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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,476	12/07/2001	Norbert O. Reich	G&C 30794.30-US-D1	8266

7590 03/29/2005

Attn: Karen S. Canady
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EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,476	REICH ET AL.	
	Examiner	Art Unit	
	Traviss C. McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-27 and 32-39* is/are pending in the application.

4a) Of the above claim(s) *36-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-27 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 10, 2005 has been entered.

The status of the claims is as follows:

The amendment filed November 9, 2004 has hereby been entered and as such, claims 28-30 have been canceled and claims 36-39 have been added. Claims 21-27 and 32-39 are pending.

Election/Restrictions

Newly submitted claims 36-39 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims as originally filed did not comprised a C-5 methylcytosine molecule only as the active agent in the method, wherein newly submitted claims 36-39 require various oligonucleotides having specific sequences as their active agent. A method of treatment using a methylcytosine molecule is not correlative to a method of treatment using a specific oligonucleotide sequence. Moreover, a reference teaching the method as claimed using a methylcytosine compound may not disclose a method of using the claimed nucleotide sequences.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 36-39 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03 and 818.02(a).

> Where claims to another invention are properly added and entered in the application before an action is given, they are treated as original claims for purposes of restriction only. The claims originally presented and acted upon by the Office on their merits determine the invention elected by an applicant in the application, and in any request for continued examination (RCE) which has been filed for the application. Subsequently presented claims to an invention other than that acted upon should be treated as provided in MPEP § 821.03.

An action on the merits of claims 21-27 and 32-35 is contained herein below.

Claim Rejections - 35 USC § 102

Applicant's arguments, in amendment filed 11/9/04, with respect to the rejection(s)of claim(s) 21-27 and 32-35 under 35 USC 102(b) have been fully considered and are persuasive. Specifically, applicants arguing that the method of Sufrin et al. was not practiced in the presence of DNA. Therefore, the rejection has been withdrawn. However, upon further consideration, a new obviousness type rejection is made in view of the same reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21, 24, and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sufrin et al. (US Patent 5,652,105).

Claim 21 is drawn to a method of inhibiting the methylation of DNA comprising contacting a DCMTase with a synthetic inhibitor molecule in the presence of DNA wherein the inhibitor molecule comprises a C-5 methylcytosine molecule which binds to an allosteric site on the DCMTase, which inhibits the methyltransferase activity. Claim 24 provides that the inhibitor is an oligonucleotide comprising the C-5 methylcytosine molecule. Claim 33 provides that the

subject is human, claim 34 provides the subject is an animal, and claim 35 provides the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine, or canine.

Sufrin et al. disclose an oligomeric DNA analog which comprises at least one 5-methylcytosine residue which specifically interacts with mammalian DCMTase (abstract). Moreover, Sufrin et al. disclose that their analogs are useful to inhibit DNA methyltransferase activity in tumor cells (column 3, lines 28-33). Sufrin et al. additionally disclose that their analogs appear to interact with both an activation and a catalytic site on the enzyme (column 7, lines 29-31). Moreover, Sufrin et al. disclose that their analogs were artificially constructed (column 4, lines 54-58). Sufrin et al. disclose that their analogs are effective in inhibiting DCMTase activity in humans (column 1, lines 42-53) as well as mice (column 2, lines 52-61).

What is not taught specifically is method being practiced in the presence of DNA nor the binding to an allosteric site on the DCMTase.

It is noted that these claims were previously rejected under 35 USC 102 as being anticipated, but since the prior art does not specifically teach binding in the presence of DNA, the claims are not seen to be anticipated.

It would have been prima facia obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Sufrin et al. in the presence of DNA. Moreover, it is noted that the step of "binding to an allosteric site" is seen to be inherently taught by Sufrin et al. as the binding of the compound to an allosteric site must have occurred in Sufrin et al. as this is a direct result of the compounds properties. That is, the instant application and Sufrin et al. both contact a 5-methylcytosine DNA with DCMTase wherein DCMTase activity was subsequently inhibited, thus the binding to an allosteric site must have inherently been performed in Sufrin et

al. Additionally, it is noted that Sufrin et al. teach their substrates to be DNA analogs comprising from 12-50 nucleobases in length (column 3, lines 4-23). Moreover, Sufrin et al. state that their analogs are specifically ascribed to their effects on DCMTase and therefore the process of DNA methylation in cells (column 3, lines 25-28). Thus, Sufrin et al. clearly suggest the use of their 5-methylcytosine containing DNA's to be used to inhibit DCMTase and thus inhibit the process of DNA methylation in cells. Moreover, Sufrin et al. state that their DNAs could be useful in treating cancers, since inhibition of DNA methylation has been shown to cause differentiation of certain types of tumor cells (column 7, lines 65-68). Thus, Sufrin et al. are clearly intending their method to be practiced in the presence of DNA, as it is well known in the art that DCMTase methylates DNA, and thus inhibiting DCMTase with their DNAs would inhibit DNA methylation.

Claims 22-23, 25-27, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sufrin et al. (US Patent 5,652,105).

Claim 22 is drawn to a method of inhibiting the proliferation of cancer cells comprising administering a synthetic inhibitor molecule that comprises a C-5 methylcytosine molecule which binds to an allosteric site on the DCMTase, which inhibits the methyltransferase activity. Claim 23 provides that the cancer is from lung, breast, prostate, pancreas, or colon. Claim 25 provides that the subject is human, claim 26 provides the subject is an animal, and claim 27 provides the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine, or canine.

Claim 32 provides that the inhibitor is an oligonucleotide comprising the C-5 methylcytosine molecule.

Sufrin et al. disclose an oligomeric DNA analog which comprises at least one 5-methylcytosine residue which specifically interacts with mammalian DCMTase (abstract). Moreover, Sufrin et al. disclose that their analogs are useful to inhibit DNA methyltransferase activity in tumor cells (column 3, lines 28-33). Sufrin et al. additionally disclose that their analogs appear to interact with both an activation and a catalytic site on the enzyme (column 7, lines 29-31). Moreover, Sufrin et al. disclose that their analogs were artificially constructed (column 4, lines 54-58). Sufrin et al. disclose that their analogs are effective in inhibiting DCMTase activity in humans (column 1, lines 42-53) as well as mice (column 2, lines 52-61). Moreover, Sufrin disclose that lowering the level and activity of DCMTase also lowers the incidence of colon cancer (column 2, lines 52-61).

What is not taught specifically is method being practiced in the presence of DNA nor the binding to an allosteric site on the DCMTase.

It is noted that these claims were previously rejected under 35 USC 102 as being anticipated, but since the prior art does not specifically teach binding in the presence of DNA, the claims are not seen to be anticipated.

It would have been prima facia obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Sufrin et al. in the presence of DNA. Moreover, it is noted that the step of "binding to an allosteric site" is seen to be inherently taught by Sufrin et al. as the binding of the compound to an allosteric site must have occurred in Sufrin et al. as this is a direct result of the compounds properties. That is, the instant application and Sufrin et al. both

contact a 5-methylcytosine DNA with DCMTase wherein DCMTase activity was subsequently inhibited, thus the binding to an allosteric site must have inherently been performed in Sufrin et al. Additionally, it is noted that Sufrin et al. teach their substrates to be DNA analogs comprising from 12-50 nucleobases in length (column 3, lines 4-23). Moreover, Sufrin et al. state that their analogs are specifically ascribed to their effects on DCMTase and therefore the process of DNA methylation in cells (column 3, lines 25-28). Thus, Sufrin et al. clearly suggest the use of their 5-methylcytosine containing DNA's to be used to inhibit DCMTase and thus inhibit the process of DNA methylation in cells. Moreover, Sufrin et al. state that their DNAs could be useful in treating cancers, since inhibition of DNA methylation has been shown to cause differentiation of certain types of tumor cells (column 7, lines 65-68). Thus, Sufrin et al. are clearly intending their method to be practiced in the presence of DNA, as it is well known in the art that DCMTase methylates DNA, and thus inhibiting DCMTase with their DNAs would inhibit DNA methylation.

The invention of claims 21-27 and 32-35 is seen to be prima facia obvious in view of the Sufrin et al. reference.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
March 18, 2005

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623